[Cited Reference 1]

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Title of Invention: A release rate controlling composition

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What Is Claimed:

[Claim 1] A release rate controlling composition in which a nucleus containing a medicament is coated with a water - insoluble substance and a swellable polymer having no basic radical.

[Claim 2] A release rate controlling composition as claimed in Claim 1 in which the water - insoluble substance has a coat - forming ability.

[Claim 3] A release rate controlling composition as claimed in Claim 1 in which the water - insoluble substance is a cellulose ether or a cellulose ester.

[Claim 4] A release rate controlling composition as claimed in Claim 1 in which the water - insoluble substance is an ethyl cellulose.

[Claim 5] A release rate controlling composition as claimed in Claim 1 in which the swellable polymer has an acidic radical and is such a polymer that may exhibit a pH dependent swelling.

[Claim 6] A release rate controlling composition as claimed in Claim 1 in which the swellable polymer is a crosslinking type acrylic acid polymer.

[Claim 7] A release rate controlling composition as claimed in Claim 5 in which the molecular weight of the swellable polymer is in the range of about 1,000,000 to about 10,000,000.

[Claim 8] A release rate controlling composition as claimed in Claim 5 in which the viscosity of the swellable polymer in a 0.2 - percent neutral solution is in the range of about 1,500 to about 60,000.

[Claim 9] A release rate controlling composition as claimed in Claim 1 in which the coating agent further contains a hydrophilic substance.

[Claim 10] A release rate controlling composition as claimed in Claim 9 in which the hydrophilic substance is a hydroxy alkyl radical or a carboxy alkyl radical.

[Claim 11] A release rate controlling composition as claimed in Claim 9 in which the hydrophilic substance is a hydroxy propyl methyl cellulose.

[Claim 12] A release rate controlling composition as claimed in Claim 1 in which the nucleus is coated with 1 percent (w / w) or more of coating agent.

[Claim 13] A release rate controlling composition as claimed in Claim 1 in which the water - insoluble substance and swellable polymer contents in the coating agent are in the range of about 40 to about 95 percent (w / w) and about 1 to about 40 percent (w / w) respectively.

[Claim 14] A release rate controlling composition as claimed in Claim 9 in which the water - insoluble substance, swellable polymer and hydrophilic polymer contents in the coating agent are in the range of about 40 to about 95 percent (w / w), about 1 to about 40 percent (w / w) and 0 to about 40 percent (w / w) respectively.

[Claim 15] A release rate controlling composition as claimed in Claim 1 in which the water - insoluble substance is an ethyl cellulose, and further in which the swellable polymer is a crosslining type acrylic acid polymer.

[Claim 16] A release rate controlling composition as claimed in Claim 1 in which the medicament is an opioide compound.

[Claim 17] A release rate controlling composition as claimed in Claim 1 in which the medicament is morphine or the salt thereof.

[Claim 18] A release rate controlling composition as claimed in Claim 1 in which the medicament is such a type that may act to the orthosympathetic system.

[Claim 19] A release rate controlling composition as claimed in Claim 1 which contains 0.5 percent (w / w) of the medicament.

[Claim 20] A release rate controlling composition as claimed in Claim 1 which is in the form of a granule, a fine particle, a tablet or a capsule.

[Claim 21] A release rate controlling composition which contains a water - insoluble substance and a swellable polymer having no basic radical.

[Claim 22] A release rate controlling composition as claimed in Claim 21 which further contains a hydrophilic substance.

[Claim 23] A process for the preparation of a release rate controlling composition in which the nucleus containing a medicament is coated with a coating

agent containing a water - insoluble substance and a swellable polymer having no basic radical.

Detailed Explanation Of The Invention

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[The Means To Solve The Problems]

The medicaments to be used in the present invention are not particularly limited, but for example, it is possible to use morphine, or pharmacologically permissible salts thereof (example, hydrochloride, sulfate and so on), hydrohormone, opiodoide compounds such as oxycodon, medadon, meperidine, dihydrocodine, codine, dihydromorphine, buprenorphine, fentanyl and so on; and anti - inflammatory drugs such as sodium naproxinate, ibuprofen, ketoprofen, dichlophenag sodium and so on ----.

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[0010] The composition of the present invention can be made by preparing a nucleus containing a medicament and thereafter coating the thus obtained nucleus with a coating agent solution obtained by heat - melting a water - insoluble substance and a swellable polymer having no basic radical or dissolving or dispersing the same in a solvent. The process for the preparation of the composition of the present invention will be explained in detail as follows:

1. Preparation of the nucleus containing the medicament:

In the case of the composition of the present invention, the shape of the nucleus containing the medicament which is coated with a coating agent (which is hereinafter referred to as simply "nucleus") is not particularly limited. For example, it is possible to mention a tablet, a round agent, a granule or a fine particle. In the case that the nucleus is a granule or a fine particle, the average particle diameter thereof is preferably in the range of about 150 to 2, 000 μ m, and more preferably in the range of about 500 to about 800 μ m. Among these ranges, in the specification of the present invention, the fine particle means those having a particle diameter of about 500 μ m or smaller. The preparation of the nucleus can be carried out according to a normal preparation method. For example, it can be prepared by mixing, with a medicament, an appropriate shape - forming agent, a bonding agent, a decay agent, a glossy agent and so on, and employing a wet type extruding particle forming method, a fluid layer particle forming method and so on. The medicament content in the nucleus is in the range of about 0.5 to about 95 percent (w / w), preferably in the range of about 5.0 to about 60 percent (w / w), more preferably in the range of about 30 to about 60m percent (w / w). As the shape - forming agent to be contained in the nucleus, it is possible to employ, for example, sugars such as white sugar, lactose, mannitol, glucose and so on; starch, crystalline cellulose, calcium phosphate and so on. As the bonding agent, it is possible to employ, for example, a polyvinyl alcohol, a hydroxy propyl cellulose, macrogaol (phonetic), pluronic F68 (phonetic), Arabian rubber, gelatine, starch and so on. As the decay agent (houkaizai), it is possible to employ, for example, a carboxy methyl cellulose calcium (ECG505), cross carbelose sodium (Ac - Di -

Sol), polyvinyl pyrroridone, a low - substitution hydroxy propyl cellulose (L - HPC) and so on. As the glossy agent (kattakuzai) and the anti - coagulation agent, it is possible to employ, for example, talc, magnesium stearate and so on.

[0011] In addition to the above - mentioned preparation methods, the nucleus can be prepared, for example, by a rolling particle forming method, a pan - coating method, a fluid layer coating method and a melting particle forming method, in which a medicament or the mixture thereof with a shape - forming agent, a glossy agent and so on is added thereto little by little, while a bonding agent dissolved in an appropriate solvent such as water, lower alcohol, (for example, methanol, ethanol and so on) is being sprayed onto an inert carrier particle which will be the center of the nucleus. As the inert carrier particle, those made of white sugar, lactose, starch, crystalline cellulose and waxes can be used, and the average particle diameter thereof is preferably in the range of about 100 μ m to about 1,500 μ m. The components of the present invention are not limited to the above - mentioned ones, and those which are permissible as a medical preparation will all do. The surface of the thus obtained nucleus can be covered with a protective agent for the purpose of separating the medicament from the coating agent. As the protective agent, it is possible to use, for example, said hydrophilic substance, a water - insoluble substance and so on. As the protective agent, it is preferable to use polysacharides having a hydroxy alkyl radical or a carboxy alkyl radical, and more preferably a hydroxy propyl methyl cellulose is used. In the case that the protective agent is used, and the coating amount in relation to the nucleus will be in the range of about 1 to about 15 percent (w / w), preferably in the range of about 1 to about 10 percent (w / w), and more preferably in the range of about 2 to about 8 percent (w / w). The protective agent can be coated according to a normal coating method, and to be more concrete, the protective agent can be spray - coated onto the nucleus according to the fluid layer coating method, the pan - coating method and so on.

[0012] II. Coating of the nucleus with a coating agent:

The composition of the present invention can be made by coating the nucleus obtained as in the above - mentioned I, with a coating agent solution obtained by heat - melting or dissolving or dispersing, into a solvent, said water - insoluble substance and a swellable agent, and if it is necessary, a hydrophilic substance. As the method of coating the nucleus with a coating agent solution, it is possible to mention the method of spray - coating the nucleus as obtained in the above - mentioned I, with the coating agent solution. The composition ratios of the water - insoluble substance, the swellable polymer or the hydrophilic substance in the coating agent solution can be appropriately selected such that the contents of the respective components in the coating may result in the above - mentioned contents. The coated amount of the coating agent in relation to the nucleus (without containing the coated amount of the protective agent) is in the range of about 1 to about 90 percent (w / w), preferably in the range of about 5 to about 50 percent (w / w), more preferably in the range of about 10 to 40 percent (w / w).